SUMMARY MINUTES

MEETING OF THE OBSTETRICS AND GYNECOLOGY DEVICES

ADVISORY PANEL

OPEN SESSION

June 9, 2003

Gaithersburg Hilton
Gaithersburg, MD

Obstetrics and Gynecology Devices Advisory Panel Meeting
Open Session June 9, 2003

Attendees

Chairperson
Mary Jo O'Sullivan, M.D.
University of Miami/Jackson Memorial Hospital

Executive Secretary
Joyce M. Whang, Ph.D.
Division of Reproductive, Abdominal, and Radiological Devices

Voting Members
Machelle Allen, M.D.
NYU School of Medicine

Carol L. Brown, M.D.
Weill-Cornell Medical College
Memorial Sloan-Kettering Cancer Center

Charles C. Coddington, III, M.D.
Department of Obstetrics and Gynecology Denver Health Medical Center

Ralph B. D'Agostino, Ph.D.
Mathematical Statistics Department
Boston University

Gary S. Eglinton, M.D.
Department of Obstetrics and Gynecology
New York Hospital Medical Center at Queens

Evelyn R. Hayes, Ph.D.
College of Health and Nursing Sciences, University of Delaware

Jay D. Iams, M.D.
Department of Obstetrics and Gynecology
Ohio State University

Kinley Larntz, Ph.D.
School of Statistics, University of Minnesota

Michael Neuman, M.D., Ph.D.
Joint Program of Biomedical Engineering
University of Memphis

Kenneth L. Noller, M.D.
Department of Obstetrics and Gynecology
Tufts University Medical School

Susan M. Ramin, M.D.
Department of Obstetrics and Gynecology and Reproductive Sciences
University of Texas–Houston Medical School

Nancy C. Sharts-Hopko, Ph.D.
College of Nursing, Villanova University

Jonathan W. Weeks, M.D.
Suburban Hospital, Maternal-Fetal Medical Center
Louisville, KY

Deborah A. Wing, M.D.
Department of Obstetrics and Gynecology
Women's and Children's Hospital and USC Medical Center

Robert N. Wolfson, M.D., Ph.D.
Specialists in Women's Health
Colorado Springs

Consumer Representative
Kleia R. Luckner, J.D., M.S.N.
The Toledo Hospital

Industry Representative
Mary Lou Mooney, R.A.C.
SenoRx, Inc.

FDA Participants
Nancy C. Brogdon
Director, Division of Reproductive, Abdominal, and Radiological Devices

Colin Pollard
Chief, Obstetrics and Gynecology Devices Branch

Danica Marinac-Dabic, M.D., M.M.Sc.
Office of Surveillance and Biometrics

CALL TO ORDER

Panel Chair Mary Jo O'Sullivan, M.D., called the open session to order at 2:49 p.m. and asked the panel members to introduce themselves. **Panel Executive Secretary Joyce Whang** noted that upcoming panel meetings have been tentatively scheduled for September 8 and 9 and November 3 and 4, 2003. The panel has four new voting members: Evelyn R. Hayes, Ph.D., Hugh Miller, M.D., Jonathan W. Weeks, M.D., and Kenneth L. Noller, M.D. in addition, Charles C. Coddington, III, M.D., and Deborah A. Wing, M.D., are new panel consultants.

Dr. Whang then read the conflict of interest statement. A full waiver had been granted to Michael Neuman, M.D., Ph.D., who reported interests in firms at issue in matters unrelated to the day's agenda. Hugh Miller, M.D., reported past interests in firms at issue in matters unrelated to the first session's agenda and could participate fully in the panel's first session. However, due to conflicts of interest in matters related to the second session's agenda, Dr. Miller was excluded from the second session.

BRANCH UPDATE

Colin Pollard, chief, Chief, Obstetrics and Gynecology Devices Branch, introduced new FDA branch staff to the panel and updated the panel on the activities of the branch since the last panel meeting. Three original PMAs have been approved: the Essure System for permanent birth control (November 2002); the Philips fetal pulse oximeter (January 2003); and the FemCap device, a barrier contraceptive (March 2003). The Essure device was approved with conditions including postapproval studies. The sponsor will continue to follow up with patients in phase 2 of the clinical trial and the pivotal study as well as conduct a smaller study to look at bilateral placement rates in the general population.

Using a new regulatory tool called *early collaboration*, the Agency has reached regulatory agreement on the pivotal clinical trial for Medispectra, an optical system intended to serve as an adjunct to colposcopy for detection and localization of diseased cervical tissue. In October 2002, the Agency approved a 510(k) for the Embosphere for uterine fibroid embolization, a nonsurgical alternative for women with symptomatic uterine fibroids. The company will follow clinical trial subjects for 3 years. In addition, In March 2003 the Agency did a *de novo* reclassification of the BreastView system, a breast lesion documentation system. Finally, the Agency oversaw the voluntary market withdrawal of Intergel, an adhesion barrier product that is applied immediately after pelvic surgery and before surgical closure.

Mr. Pollard stated that the purpose of the meeting was to update the panel on the status of postapproval studies on the OxiFirst intrapartum fetal pulse oximeter.

OPEN PUBLIC HEARING

No comments were made.

OXIFIRST POSTAPROVAL STUDIES AND ADVERSE EVENTS

Danica Marinac-Dabic, M.D., M.M.Sc., Office of Surveillance and Biometrics, presented an update on FDA's post-market surveillance activities related to the OxiFirst fetal Oxygen Saturation Monitoring System. She reviewed the original approval decision and outlined the issues that needed to be addressed in the postapproval studies for Nellcor's OxiFirst device, which include the indications, cesarean section rates, maternal infection rates, duration for which oxygen saturation can remain below 30 percent before the risk of fetal injury, adequacy of labor, and neonatal outcomes.

The postapproval plan has evolved into three separate studies: a General Use Study, a Dystocia Study, and a Fetal Oximeter (FOX) Trial.

From July 2000 to June 2003, an estimated 15,000 patients were monitored, and 14 adverse events were reported. The adverse events resulted in three deaths and nine injuries; two of the events involved device malfunctions. Five of the adverse event reports indicated clear deviation from the clinical guidelines.

A September 2001 ACOG committee opinion may have affected the use of the device; the opinion stated that the committee could not endorse use of the device because doing so could increase the cost of care without improving clinical outcomes. In October 2002, Nellcor stopped active marketing of the device and is now servicing only existing customers. Dr. Dabic reminded the panel that the 14 adverse event reports came from passive surveillance, meaning that it is highly likely that adverse events are underreported.

The sponsor submitted a PMA supplement to change the labeling for the device; it was approved in November 2002. The changes expanded the definitions of "ominous" FHR and added a footnote stating that it is not necessary to wait for more than 7 minutes of prolonged deceleration before initiating intervention, even with reassuring $FSpO_2$. The labeling changes also stated that when $FSpO_2$ is not available, the fetus should be managed by FHR and clinical signs alone; that OxiFirst is to be used as an adjunct to FHR monitoring, and that FHR classification and clinical management tables accompanying the device are recommendations.

In February 2003, the company sent a "Dear Doctor" letter to clinical users of the device; the letter informed clinicians of the labeling changes. FDA also sent a letter to the National Institute of Child Health and Human Development (NICHD); it highlighted the issues in the Dear

Doctor letter and stated that the changes do not undermine the results of the pivotal trial. When used according to the labeling, the device is safe and effective for its intended use.

Dr. Dabic then summarized the status of the three studies. The General Use Study is currently on hold because the usage rate is 1 percent of all births; therefore, accrual of study participants is not proceeding at the anticipated pace. The final report for the Dystocia Study, which involved 274 patients at 5 sites, is in preparation. The FOX Trial, which is being conducted by the NICHD Maternal Fetal Medicine Unit (MFMU), is under way; current enrollment is 1,026, and the anticipated sample size is approximately 10,000. The study is expected to last 2 to 3 years.

Catherine Y. Spong, M.D., chief, Pregnancy and Perinatology Branch of the National Institutes of Health, described the NICHD FOX study. The aim of the study is to determine whether fetal pulse oximetry affects the total Cesarean delivery rate. Participant recruitment began in May 2002; more than 6,000 patients have been screened, 38 percent of whom were ineligible. The consent rate is 30 percent. The mean age of participants is 23.2 years and the mean education is 12.2 years; 6.6 percent are smokers. A total of 49.3 percent are white, and 29.6 percent are Hispanic/Latino.

David Swedlow, M.D., consultant to Nellcor Puritan Bennett, began by showing the numbers of monitors and sensors shipped over time. He noted that clinicians who were using the OxiFirst device use it at same rate as before the ACOG statement. Adverse events occurred during early use, but as experience increased, events have tapered off. The sponsor introduced new software and guidelines for use in fall 2002. All NICHD sites are using the new software.

The Dystocia Study is testing the hypothesis that significantly more nonreassuring FHR patterns identify patients at an increased risk for dystocia given an adequate trial of labor in a

setting of fetal well-being defnied by normal fetal pulse oximetry. The study divided FHR into two classes: intermittent, mildly nonreassuring (Class I) and persistent, progressive, moderate to severe nonreassuring (Class II). The study found that significantly more patients in Class II than in Class I had cesarean delivery, confirming the hypothesis. The two groups were not significantly different on a number of other variables.

The General Use Study was designed to address the concern that widespread uncontrolled use of FSpO2 could increase the C-section rate. A prospective 3-site study has been initiated to compare C-section rate with the use of Oxifirst to historical rates. However, C-section rates have changed in the time needed to initiate the study. The useage rate has turned out to be about 1%, which is much less than the 30% projected when the study was designed. At the current rate of accrual, it would take three decades to complete.

Panel members asked clarifying questions on various aspects of the methodology of the three studies. Ms. Brogdon noted that the Agency has to decide whether to cancel certain conditions of approval. Panel members noted that it has been difficult for the company to comply with the conditions and that no decision could be made before the NICHD trial ends.

ADJOURNMENT

Dr. O'Sullivan thanked the participants and adjourned the meeting at 4:08 p.m.

I certify that I attended this open session of the Obstetrics and Gynecology Devices Advisory Panel Meeting on June 9, 2003, and that these minutes accurately reflect what transpired.

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Joyce M. Whang, Ph.D.
Executive Secretary

I approve the minutes of this meeting as recorded in this summary.

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Mary Jo O'Sullivan, M.D.
Chairperson

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